STN Search History

FILE 'HOME' ENTERED AT 08:25:44 ON 09 FEB 2004

L1 5036 (HEMATOPOIESIS OR HAEMATOPOIESIS OR POLYCYTHEMIA OR (HEMATO#####
OR HAEMOTO########) (A) PROLIFERAT######) (S) (INHIBIT####
OR PREVENT######)

L2 0 L1 AND (QQY OR GLU-GLU-TYR OR GLUTA#### (3A) GLUTAM### (3A)
TYROSINE)

L8 327 L7 AND((HEMATOLOGIC### OR CELL OR HAEMATOLOGIC####) (S) PROLIFE
RAT#### OR POLYCYTHEMIA)

L11 184 L9 AND ((PEPTIDE OR PROTEIN OR POLYPEPTIDE) (S) (HEMATOPOIESIS
OR HAEMATOPOIESIS OR PROLIFERAT######))

L12 45 L9 AND ((PEPTIDE OR PROTEIN OR POLYPEPTIDE) (S) (INHIBIT OR
PREVENT) (S) (HEMATOPOIESIS OR HAEMATOPOIESIS OR PROLIFERAT#####
#))

(FILE 'HOME' ENTERED AT 08:25:44 ON 09 FEB 2004)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH' ENTERED AT 08:27:20 ON
09 FEB 2004

L1 5036 S (HEMATOPOIESIS OR HAEMATOPOIESIS OR POLYCYTHEMIA OR (HEMATO##
L2 0 S L1 AND (QQY OR GLU-GLU-TYR OR GLUTA#### (3A) GLUTAM### (3A)
L3 4260 S L1 NOT PY>2001
L4 1078 S L1 AND (HEMATOPOIESIS OR HAEMATOPOIESIS OR POLYCYTHEMIA OR (H
L5 0 S L4 AND (HEMATO########## OR HAEMATO############)/ABS
L6 940 S L4 AND (HEMATO########## OR HAEMATO############)/AB
L7 888 S L6 AND (INHIBIT###### OR REDUC###### OR TREAT#####)/AB
L8 327 S L7 AND((HEMATOLOGIC### OR CELL OR HAEMATOLOGIC####) (S) PRO
L9 189 DUP REM L8 (138 DUPLICATES REMOVED)
L10 184 S L9 AND (PEPTIDE OR PROTEIN OR POLYPEPTIDE)/AB
L11 184 S L9 AND ((PEPTIDE OR PROTEIN OR POLYPEPTIDE) (S) (HEMATOPOIES
L12 45 S L9 AND ((PEPTIDE OR PROTEIN OR POLYPEPTIDE) (S) (INHIBIT OR

ANSWER 45 OF 45 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

AN 97:690793 SCISEARCH

GA The Genuine Article (R) Number: XV845

TI CBF beta-SMMHC, expressed in M4Eo AML, reduced CBF DNA-binding and inhibited the G1 to S cell cycle transition at the restriction point in myeloid and lymphoid cells

AU Cao W S; BritosBray M; Claxton D F; Kelley C A; Speck N A; Liu P P; Friedman A D (Reprint)

CS JOHNS HOPKINS UNIV, CTR ONCOL, DIV PEDIAT ONCOL, 600 N WOLFE ST, BALTIMORE, MD 21287 (Reprint); JOHNS HOPKINS UNIV, CTR ONCOL, DIV PEDIAT ONCOL, BALTIMORE, MD 21287; UNIV TEXAS, DEPT HEMATOL, HOUSTON, TX 77030; NHLBI, NIH, BETHESDA, MD 20892; DARTMOUTH COLL, SCH MED, DEPT BIOCHEM, HANOVER, NH 03755; NIH, NATL CTR HUMAN GENOME RES, BETHESDA, MD 20892

CYA USA

SO ONCOGENE, (11 SEP 1997) Vol. 15, No. 11, pp. 1315-1327.
Publisher: STOCKTON PRESS, HOUNDMILLS, BASINGSTOKE, HAMPSHIRE, ENGLAND RG21 6XS.
ISSN: 0950-9232.

DT Article; Journal

FS LIFE

LA English

REC Reference Count: 67

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB CBF beta-SMMHC is expressed from the inv(16) chromosome in M4Eo AML. Mice lacking CBF subunits or expressing the CBF beta-SMMHC or AML1-ETO onco-**proteins** failed to develop definitive **hematopoiesis**. To investigate these effects on **hematopoiesis**, we expressed CBF beta-SMMHC from the metallothionein promoter, in both 32D c13 myeloid **cells** and Ba/F3 B-lymphoid **cells**. Addition of zinc increased CBF beta-SMMHC levels more than tenfold, with higher levels evident in Ba/F3 lines. Levels obtained in 32D c13 **cells** were similar to those of endogenous CBF beta. Indirect immunofluorescence revealed zinc-inducible speckled, nuclear staining in Ba/F3 **cells** and diffuse nuclear staining in 32D c13 **cells**. CBF beta-SMMHC **reduced** endogenous CBF DNA-binding fivefold in both **cell** types, increased **cell** generation time 1.9-fold, on average, in 32D c13 **cells** and 1.5-fold in Ba/ F3 **cells** and decreased tritiated thymidine incorporation into DNA correspondingly. CBFP beta-SMMHC increased the proportion of **cells** in G1 1.7-fold, on average, in 32D c13 and Ba/F3 **cells**, and decreased the proportion of **cells** in S phase by a similar degree. CBF beta-SMMHC induced a marked increase in hypophosphorylated Rb, but did not alter IL-3 Receptor alpha or beta subunit levels. Neither apoptosis nor 32D differentiation was induced by zinc in IL-3 in these lines. Induction of CBF beta-SMMHC WC in 32D c13 **cells** did not **inhibit** their differentiation to neutrophils or their expression of myeloperoxidase mRNA in GCSF, and did not produce an eosinophilic phenotype. Additional, **proliferative** genetic changes in M4eo AMLs might potentiate **inhibition** of differentiation by CBF beta-SMMHC by allowing its increased expression.

L12 ANSWER 39 OF 45 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 92082253 EMBASE
DN 1992082253
TI The identification and characterization of a novel human differentiation-inhibiting protein that selectively blocks erythroid differentiation.
AU Durkin J.P.; Biquard J.M.; Whitfield J.F.; Morardet N.; Royer J.; Macdonald P.; Tremblay R.; Legal J.D.; Doyonnas R.; Blanchet J.P.; Krsmanovic V.
CS Cell Signals Group, Biological Sciences Institute, Natl. Res. Council of Canada,Ottawa, Ont., Canada
SO Blood, (1992) 79/5 (1161-1171).
ISSN: 0006-4971 CODEN: BLOOAW
CY United States
DT Journal; Article
FS 025 Hematology
030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB We have isolated a novel **inhibitor** of erythropoietic differentiation from the plasma of a patient suffering from idiopathic pure red **cell** aplasia. This differentiation-**inhibiting** **protein** (DIP) specifically blocked the differentiation of human burst-forming unit-erythroid (BFU-E), but not colony-forming unit-erythroid (CFU-E) **cells**. DIP also blocked the maturation of murine BFU-E **cells**, but not CFU-E or CFU-granulocyte-macrophage **cells**, and it **inhibited** the dimethyl sulfoxide (DMSO)-induced differentiation of Friend murine erythroleukemia **cells** (FLC) at levels between 10-10 and 10-12 mol/L. DIP activity was not detectable in the plasma of normal, healthy subjects. Unlike other known **inhibitors** of **hematopoiesis**, DIP appears to directly **inhibit** erythropoietic differentiation, because it did not affect the **proliferation** of untreated FLC and it effectively blocked FLC hemoglobinization without affecting the ability of the blocked **cells** to **proliferate**. DIP blocked FLC differentiation only when added to the culture medium within 1 hour of inducing the **cells** with DMSO, suggesting that the **protein** **inhibited** an early, but critical, DMSO-induced cellular process. DIP appears to be at least partially responsible for the patient's anemia, and its unique activity suggests a role in the early development of some erythroleukemias.

L12 ANSWER 36 OF 45 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 93083827 EMBASE
DN 1993083827
TI Use of 5-fluorouracil to analyze the effect of macrophage inflammatory protein-1α on long-term reconstituting stem cells in vivo.
AU Quesniaux V.F.J.; Graham G.J.; Pragnell I.; Donaldson D.; Wolpe S.D.; Iscove N.N.; Fagg B.
CS Preclinical Research, Sandoz Pharma Ltd,4002 Basel, Switzerland
SO Blood, (1993) 81/6 (1497-1504).
ISSN: 0006-4971 CODEN: BLOOAW
CY United States
DT Journal; Article
FS 025 Hematology
030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB A macrophage-derived **inhibitor** of early **hematopoietic** progenitors (colony- forming unit-spleen, CFU-A) called stem cell **inhibitor** was found to be identical to macrophage inflammatory **protein**-1α (MIP-1α). We investigated the effect of MIP-1α on the earliest stem cells that sustain long-term **hematopoiesis** in vivo in a competitive bone marrow repopulation assay. Because long-term reconstituting (LTR) stem cells are normally quiescent, an in vivo model was first developed in which they are triggered to cycle. A first 5-fluorouracil (5-FU) injection was used to eliminate later progenitors, causing the LTR stem cells, which are normally resistant to 5- FU, to enter the cell cycle and become sensitive to a second 5-FU injection administered 5 days later. Human MIP-1α administered from day 0 to 7 was unable to **prevent** the depletion of the LTR stem cells by the second 5-FU **treatment**, as observed on day 7 in this model, suggesting that the LTR stem cells were not **prevented** from being triggered into cycle despite the MIP-1α **treatment**. However, the MIP-1α protocol used here did substantially decrease the number of more mature **hematopoietic** progenitors (granulocyte-macrophage colony-forming cells [CFC], burst-forming unit-erythroid, CFC(multi), and pre-CFC(multi)) recovered in the bone marrow shortly after a single 5-FU injection. In vitro, MIP-1α had no **inhibitory** effect on the ability of these progenitors to form colonies. This study confirms the in vivo **inhibitory** effect of MIP-1α on subpopulations of **hematopoietic** progenitors that are activated in myelodepressed animals. However, MIP-1α had no effect on the long-term reconstituting stem cells in vivo under conditions in which it effectively **reduced** all later progenitors.

L12 ANSWER 31 OF 45 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
AN 95104915 EMBASE
DN 1995104915
TI Transforming growth factor β1 inhibits expression of the gene products for steel factor and its receptor (c-kit).
AU Heinrich M.C.; Dooley D.C.; Keeble W.W.
CS 3710 SW US Veterans Hospital Rd,Portland, OR 97207, United States
SO Blood, (1995) 85/7 (1769-1780).
ISSN: 0006-4971 CODEN: BLOOAW
CY United States
DT Journal; Article
FS 025 Hematology
LA English
SL English
AB Transforming growth factor β1 (TGF-β1), a product of marrow stromal **cells**, **inhibits** the **proliferation** and differentiation of **hematopoietic** progenitor **cells** within the **hematopoietic** microenvironment. Steel factor (SF), also a product of marrow stromal **cells**, is an essential positive regulator of **hematopoiesis** in vivo. TGF-β1 has been shown to repress human and murine leukemic **cell** and murine lin- bone marrow mononuclear **cell** expression of the receptor for SF (c-kit). We speculated that TGF-β1 might exert its **inhibitory** effect on **hematopoiesis** in part by decreasing SF/c-kit interactions. Therefore, we tested the hypothesis that TGF-β1 **inhibits** both stromal **cell** expression of SF and **hematopoietic** progenitor **cell** expression of c-kit. We measured stromal **cell** expression of SF **protein** and **hematopoietic** progenitor **cell** expression of membrane-bound c-kit before and after exposure to recombinant human TGF-β1. Both stromal **cell** expression of SF **protein** and **hematopoietic** progenitor **cell** expression of c-kit **protein** were **inhibited** 50% to 80% by TGF-β1. Using Northern blot and ribonuclease protection assays, we determined that TGF-β1 repressed stromal **cell** SF mRNA, but did not alter SF transcript stability. TGF-β1 was also found to repress c-kit mRNA in human leukemic myeloblasts as well as in normal lin- **hematopoietic** progenitor **cells**. In contrast with its effect on SF mRNA, TGF-β1 accelerated the degradation of c-kit mRNA. We conclude that TGF-β1 **inhibits** stromal **cell** production of SF by repression of SF gene transcription and represses **hematopoietic** progenitor **cell** expression of c-kit by decreasing the stability of c-kit transcripts. Taking into account the importance of SF and c-kit in maintaining steady-state **hematopoiesis** in vivo, the dual effect of TGF-β1 on both SF and c-kit gene expression is likely to be one of the major mechanisms by which TGF-β1 **inhibits** **hematopoiesis** in vivo.

L12 ANSWER 30 OF 45 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 95222382 EMBASE
DN 1995222382
TI Direct adhesion to bone marrow stroma via fibronectin receptors inhibits hematopoietic progenitor proliferation.
AU Hurley R.W.; McCarthy J.B.; Verfaillie C.M.
CS Dept. of Medicine, UMHC, Box 480, 420 Delaware Street SE,Minneapolis, MN 55455, United States
SO Journal of Clinical Investigation, (1995) 96/1 (511-519).
ISSN: 0021-9738 CODEN: JCINAO
CY United States
DT Journal; Article
FS 005 General Pathology and Pathological Anatomy
LA English
SL English
AB In long-term bone marrow cultures, stroma-adherent progenitors **proliferate** significantly less than nonadherent progenitors. Thus, close progenitor- stroma interactions may serve to regulate or restrict rather than promote **hematopoietic** progenitor **proliferation**. We hypothesized that signaling through adhesion receptors on **hematopoietic cells** may contribute to the **inhibition** of **proliferation** observed when progenitors are in contact with stroma. We demonstrate that progenitors cultured physically separated from stroma in a transwell **proliferate** significantly more than progenitors adherent to stroma. Furthermore, **proliferation** of colony forming **cells** (CFC) is **reduced** after specific adhesion to stroma, metabolically inactivated glutaraldehyde-fixed stroma, stromal-extracellular matrix, or the COOH- terminal heparin-binding domain of fibronectin. Nonspecific adhesion to poly- L-lysine fails to **inhibit** CFC **proliferation**. That the VLA-4 integrin is one of the receptors that transfers **proliferation inhibitory** signals was shown using blocking anti-α4 monomeric F(ab) fragments. Furthermore, when synthetic **peptides** representing specific **cell** attachment sites within the heparin-binding domain of fibronectin were added to Dexter-type marrow cultures, significantly increased recovery and **proliferation** of CFC was observed, suggesting that these **peptides** disrupt adhesion-mediated **proliferation inhibitory** events. Thus, negative regulation of **hematopoiesis** may not only depend on the action of growth **inhibitory** cytokines but also on growth **inhibitory** signals resulting from direct adhesive interactions between progenitors and marrow stroma.

on STN
AN 97070445 EMBASE
DN 1997070445
TI Reduction in the duration of myelotoxicity associated with radioimmunotherapy with infusions of the hemoregulatory peptide, HP5b in mice.
AU Alisauskas R.M.; Goldenberg D.M.; Sharkey R.M.; Blumenthal R.D.
CS R.D. Blumenthal, Ctr. for Molecular Med./Immunology, 520 Belleville Avenue, Belleville, NJ 07109, United States
SO International Journal of Cancer, (1997) 70/3 (323-329).
Refs: 31
ISSN: 0020-7136 CODEN: IJCNAW
CY United States
DT Journal; Article
FS 016 Cancer
023 Nuclear Medicine
025 Hematology
030 Pharmacology
LA English
SL English
AB The hemoregulatory **peptide**, pGlu-Glu-Asp-Cys-Lys (pEEDCK or HP5b), has been shown to reversibly **inhibit** the **proliferation** of bone-marrow progenitor **cells**, and has been reported to protect mice from the myelotoxicity associated with ara-C, a chemotherapeutic agent. We undertook to use this reagent to **reduce** radioimmunotherapy(RAIT)-associated bone-marrow toxicity by suppressing **hematopoiesis** during the critical period when bone marrow is exposed to radiation. The reported studies optimize the use of HP5b to **reduce** the duration of neutropenia and thrombocytopenia. We found that 3.6 μg/day of HP5b administered through a continuous 7d mini-osmotic pump, together with a bolus dose of 3.6 μg 3 hours before the radioantibody dose, gave the best effect, as measured by neutrophil counts on day 28 post RAIT. With sub-lethal doses of RAIT, the period of neutropenia was **reduced** by 2 weeks, and there appeared to be more rapid recovery of morphologically mature myeloid **cells**. The **peptide**, however, does not appear to alleviate the lymphotoxicity associated with RAIT. No adverse effects have been noted from continuous infusions of the **peptide**. In the past, we reported that cytokines (IL-1/GM-CSF) are not marrow-restorative when given after RAIT. However, an additive effect is observed when HP5b infusions are combined with post-RAIT cytokine administration, suggesting that a significant pool of bone-marrow progeniter **cells** remains when HP5b is co-administered with RAIT. Thus, HP5b is an alternate approach to **reducing** myelotoxicity, and may be used in combination with cytokines to further **reduce** the duration of myelosuppression.

L12 ANSWER 1 OF 45 MEDLINE on STN
AN 95002925 MEDLINE
DN 95002925 PubMed ID: 7919333
TI Distinct and overlapping direct effects of macrophage inflammatory protein-1 alpha and transforming growth factor beta on hematopoietic progenitor/stem cell growth.
AU Keller J R; Bartelmez S H; Sitnicka E; Ruscetti F W; Ortiz M; Gooya J M; Jacobsen S E
CS Biological Carcinogenesis and Development Program, Program Resources, Inc/DynCorp, National Cancer Institute (NCI)-Frederick Cancer Research and Development Center, MD 21702-1201.
SO BLOOD, (1994 Oct 1) 84 (7) 2175-81.
Journal code: 7603509. ISSN: 0006-4971.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199411
ED Entered STN: 19941222
Last Updated on STN: 19941222
Entered Medline: 19941107
AB Both transforming growth factor beta (TGF beta) and macrophage inflammatory **protein** 1 alpha (MIP-1 alpha) have been shown to be multifunctional regulators of **hematopoiesis** that can either **inhibit** or enhance the growth of **hematopoietic** progenitor cells (HPC). We report here the spectrum of activities of these two cytokines on different **hematopoietic** progenitor and stem cell populations, and whether these effects are direct or indirect. MIP-1 alpha enhances interleukin-3 (IL-3)/and granulocyte-macrophage colony-stimulating factor (GM-CSF)/induced colony formation of normal bone marrow progenitor cells (BMC) and lineage-negative (Lin-) progenitors, but has no effect on G-CSF or CSF-1/induced colony formation. Similarly, TGF beta enhances GM-CSF/induced colony formation of normal BMC and Lin- progenitors. In contrast, TGF beta **inhibits** IL-3/ and CSF-1/induced colony formation of Lin- progenitors. The effects of MIP-1 alpha and TGF beta on the growth of Lin- progenitors were direct and correlate with colony formation in soft agar. Separation of the Lin- cells into Thy-1 and Thy-1lo subsets showed that the growth of Thy-1lo Lin- cells is directly **inhibited** by MIP-1 alpha and TGF beta regardless of the cytokine used to stimulate growth (IL-3), GM-CSF, or CSF-1). In contrast, two other stem cell populations (0% to 15% Hoechst 33342/Rhodamine 123 [Ho/Rh123] and Lin-Sca-1+ cells) were markedly **inhibited** by TGF beta and unaffected by MIP-1 alpha. Furthermore, MIP-1 alpha has no effect on high **proliferative** potential colony-forming **cells** 1 or 2 (HPP-CFC/1 or /2) colony formation in vitro, whereas TGF beta **inhibits** both HPP-CFC/1 and HPP-CFC/2. Thus, MIP-1 alpha and TGF beta are direct bidirectional regulators of HPC growth, whose effects are dependent on other growth factors present as well as the maturational state of the HPC assayed. The spectrum of their **inhibitory** and enhancing activities shows overlapping yet distinct effects.

L12 ANSWER 3 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:368128 CAPLUS
DN 133:9083
TI Use of parvovirus capsid particles in the inhibition of **cell proliferation** and migration
IN Broliden, Kristina; Westgren, Magnus
PA Tripep AB, Swed.

SO PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000030668	A2	20000602	WO 1999-IB2112	19991123
	WO 2000030668	A3	20001109		
	W: AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	SE 9804022	A	20000525	SE 1998-4022	19981124
	SE 520177	C2	20030603		
	EP 1131085	A2	20010912	EP 1999-968407	19991123
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2003516927	T2	20030520	JP 2000-583551	19991123
	NO 2001002534	A	20010629	NO 2001-2534	20010523
PRAI	SE 1998-4022	A	19981124		
	WO 1999-IB2112	W	19991123		

AB The invention described herein relates to the discovery of methods and compns. for the **inhibition** of growth and/or migration of cells that have the P antigen, including but not limited to, cells of **hematopoietic** origin and endothelial cells. More specifically, parvovirus capsid particles or fragments of parvovirus capsid **proteins** are used to manufacture medicaments that can be administered to a subject to **inhibit hematopoietic** progenitor **cell** growth (e.g., prior to stem **cell** transplantation), endothelial **cell** growth, (e.g., as an anti-tumorigenesis **treatment** or to **prevent** restenosis or fibrotic build up following prosthetic implantation), or to **prevent** disorders that involve the abnormal **proliferation** of **cells** that have the P antigen (e.g., **polycythemia** vera).

L12 ANSWER 4 OF 45 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1993:552091 CAPLUS
DN 119:152091
TI Hemoregulatory peptides and pharmaceutical composition containing them
IN Bhatnagar, Pradip Kumar; Huffman, William Francis
PA SmithKline Beecham Corp., USA
SO PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9310807	A1	19930610	WO 1992-US10070	19921124
	W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, PT, RO, RU, SD, SE, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
	AU 9331452	A1	19930628	AU 1993-31452	19921124
	AU 666345	B2	19960208		

	ZA 9209084	A	19930813	ZA 1992-9084	19921124
	JP 07501543	T2	19950216	JP 1992-510187	19921124
	JP 2744133	B2	19980428		
	EP 671931	A1	19950920	EP 1992-925373	19921124
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	ES 2052447	B1	19950116	ES 1992-2524	19921214
	ES 2052447	A1	19940701		
	CN 1088935	A	19940706	CN 1993-100474	19930102
	CN 1034735	B	19970430		
	NO 9401950	A	19940725	NO 1994-1950	19940525
	US 5760003	A	19980602	US 1994-244415	19940525
PRAI	US 1991-799465		19911126		
	WO 1992-US10070		19921124		

OS MARPAT 119:152091

AB Novel peptides which have hemoregulatory activities and can be used to **inhibit** the myelopoietic system of mammals are disclosed. The **peptides**, by **inhibiting hematopoiesis**, tend to **prevent** quiescent cells from entering into cell division and so becoming susceptible to attack by cytotoxic anticancer drugs. They may also be used to arrest **proliferation** of cancer **cells** related to the myelopoietic system, i.e. myeloid leukemia. PGlu-Glu-Asp-Abu-Lys (I) (Abu=aminoburytic acid) was prepared from BOC-Lys(Cl-Z)PAM resin with a peptide synthesizer using standard procedures. A tablet contained I 40, corn starch 20, alginic acid 20, Na alginate 20, Mg stearate 1.3 mg.

L12 ANSWER 12 OF 45 EMBASE
on STN

AN 2002353566 EMBASE

TI Negative feedback on the effects of stem cell factor on hematopoiesis is partly mediated through neutral endopeptidase activity on substance P: A combined functional and proteomic study.

AU Joshi D.D.; Dang A.; Yadav P.; Qian J.; Bandari P.S.; Chen K.; Donnelly R.; Castro T.; Gascon P.; Haider A.; Rameshwar P.

CS P. Rameshwar, UMDNJ-New Jersey Medical School, MSB, 185 South Orange Ave, Newark, NJ 07103, United States. rameshwa@umdnj.edu

SO Blood, (1 Nov 2001) 98/9 (2697-2706).
Refs: 44
ISSN: 0006-4971 CODEN: BLOOAW

CY United States

DT Journal; Article

FS 025 Hematology
029 Clinical Biochemistry

LA English

SL English

AB **Hematopoietic** regulation is a complex but dynamic process regulated by intercellular and intracellular interactions within the bone marrow (BM) microenvironment. Through neurokinin-1 (NK-1) and NK-2 receptors, **peptides** (eg, substance P [SP]) encoded by the preprotachykinin-I gene mediate distinct **hematopoietic** effects. Cytokines, associated with **hematopoietic** stimulation, and SP regulate the expression of each other in BM mesenchymal and immune **cells**. Neutral endopeptidase (NEP) uses SP as a substrate to produce SP(1-4), which **inhibits** the **proliferation** of matured myeloid progenitor. This study determines whether the degradation of SP to SP(1-4) by endogenous NEP in BM stroma could be a feedback on **hematopoietic** stimulation by stem **cell** factor (SCF). SP(1-4) induced the production of transforming growth factor (TGF)-β and tumor necrosis factor-α in BM stroma. TGF-β production accounted for part of the **inhibitory** effects by SP(1-4) on the

proliferation of early (granulocyte-macrophage colony-forming units) and late (long-term culture-initiating **cells**) **hematopoietic** progenitors. Enzyme-linked immunosorbent assays and/or proteinchip arrays indicated a timeline change of SP to SP(1-4) in BM stroma stimulated with SCF, which correlated with increase in NEP messenger RNA. Since SP and its fragment, SP(1-4), interact with the same receptor to mediate opposing **hematopoietic** effects, 2 interactive studies were done to understand the dual responses of NK-1: (1) a 3-dimensional molecular model of NK-1 and SP and (2) screening of a random dodecapeptide library for SP(1-4) interacting sites. The effects of SP(1-4) on **hematopoietic** progenitors and the timeline change of SP to SP(1-4), together with the 3-dimensional model, provide a partial explanation for the feedback on the stimulatory effects of SCF and SP on **hematopoiesis**. .COPYRGT. 2001 by The American Society of **Hematology**.

L12 ANSWER 14 OF 45 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 2001036135 EMBASE
TI Interleukin 6 inhibits **proliferation** and, in cooperation with an epidermal growth factor receptor autocrine loop, increases migration of T47D breast cancer **cells**.
AU Badache A.; Hynes N.E.
CS A. Badache, Friedrich Miescher Institute, P.O. Box 2543, CH-4002 Basel, Switzerland. badache@fmi.ch
SO Cancer Research, (1 Jan 2001) 61/1 (383-391).
Refs: 45
ISSN: 0008-5472 CODEN: CNREA8
CY United States
DT Journal; Article
FS 016 Cancer
LA English
SL English
AB Interleukin (IL)-6, a multifunctional regulator of immune response, **hematopoiesis**, and acute phase reactions, has also been shown to regulate cancer **cell proliferation**. We have investigated IL-6 signaling pathways and cellular responses in the T47D breast carcinoma **cell** line. The IL-6-type cytokines, IL-6 and oncostatin M, simultaneously **inhibited cell proliferation** and increased **cell** migration. In T47D **cells**, IL-6 stimulated the activation of Janus-activated kinase 1 tyrosine kinase and signal transducers and activators of transcription (STAT) 1 and STAT3 transcription factors. Expression of dominant negative STAT3 in the **cells** strongly **reduced** IL-6-mediated growth **inhibition** but did not **prevent** IL-6-induced **cell** migration. IL-6 **treatment** led to activation of the mitogenactivated **protein** kinase (MAPK) and the phosphatidylinositol 3'-kinase (PI3K) pathways. **Inhibition** of MAPK or PI3K activity reversed IL-6- and oncostatin M-stimulated migration. Because cross-talk between cytokine receptors and members of the ErbB family of receptor tyrosine kinases has been described previously, we have examined their interaction in T47D **cells**. Down-regulation of ErbB receptor activity, through the use of specific pharmacological **inhibitors** or dominant negative receptor constructs, revealed that IL-6-induced MAPK activation was largely dependent on epidermal growth factor (EGF) receptor activity, but not on ErbB-2 activity. Using a monoclonal antibody that interferes with EGF receptor-ligand interaction, we have shown that in T47D **cells**, IL-6 cooperates with an EGF receptor autocrine activity loop for signaling through the MAPK and PI3K pathways and for **cell** migration. Both the tyrosine phosphatase SHP-2 and the multisubstrate docking molecule

Gab1, which are potential links between IL-6 and the MAPK/PI3K pathways, were constitutively associated with the active EGF receptor. On IL-6 stimulation, SHP-2 and Gab1 were recruited to the gp130 subunit of the IL-6 receptor and tyrosine phosphorylated, allowing downstream signaling to the MAPK and PI3K pathways. Thus, in T47D breast carcinoma **cells**, IL-6 acts in synergy with EGF receptor autocrine activity to signal through the MAPK/PI3K pathways. Cooperation between IL-6 and the EGF receptor in T47D breast carcinoma **cells** illustrates how a combination of multiple stimuli, either exogenous or endogenous, may result in synergistic cellular responses.

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AN 2000046840 EMBASE

TI Expression of interferon consensus sequence binding protein (ICSBP) is downregulated in Bcr-Abl-induced murine chronic myelogenous leukemia-like disease, and forced coexpression of ICSBP inhibits Bcr-Abl-induced myeloproliferative disorder.

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SO Molecular and Cellular Biology, (2000) 20/4 (1149-1161).
Refs: 45
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CY United States

DT Journal; Article

FS 025 Hematology
029 Clinical Biochemistry

LA English

SL English

AB Chronic myelogenous leukemia (CML) is a clonal myeloproliferative disorder resulting from the neoplastic transformation of a **hematopoietic** stem **cell**. The majority of cases of CML are associated with the (9;22) chromosome translocation that generates the bcr-abl chimeric gene. Alpha interferon (IFN-α) **treatment** induces **hematological** remission and prolongs life in 75% of CML patients in the chronic phase. It has been shown that mice deficient in interferon consensus sequence binding **protein** (ICSBP), a member of the interferon regulatory factor family, manifest a CML-like syndrome. We have shown that expression of Bcr-Abl in bone marrow (BM) **cells** from 5- fluorouracil (5-FU)-**treated** mice by retroviral transduction efficiently induces a myeloproliferative disease in mice resembling human CML. To directly test whether icsbp can function as a tumor suppressor gene, we examined the effect of ICSBP on Bcr-Abl-induced CML-like disease using this murine model for CML. We found that expression of the ICSBP **protein** was significantly decreased in Bcr-Abl-induced CML-like disease. Forced coexpression of ICSBP **inhibited** the Bcr-Abl-induced colony formation of BM **cells** from 5-FU-**treated** mice in vitro and Bcr-Abl-induced CML-like disease in vivo. Interestingly, coexpression of ICSBP and Bcr-Abl induced a transient B- lymphoproliferative disorder in the murine model of Bcr-Abl-induced CML-like disease. Overexpression of ICSBP consistently promotes rather than **inhibits** Bcr-Abl-induced B lymphoproliferation in a murine model where BM **cells** from non-5-FU-**treated** donors were used, indicating that ICSBP has a specific antitumor activity toward myeloid neoplasms. We also found that overexpression of ICSBP negatively regulated normal **hematopoiesis**. These data provide direct evidence that ICSBP can act as a tumor suppressor that regulates normal and neoplastic **proliferation** of **hematopoietic** **cells**.

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on STN
AN 1998002442 EMBASE
TI Inhibition of interferon regulatory factor-1 expression results in predominance of cell growth stimulatory effects of interferon-γ due to phosphorylation of Stat1 and Stat3.
AU Sato T.; Selleri C.; Young N.S.; Maciejewski J.P.
CS Dr. J.P. Maciejewski, Department of Microbiology, Howard Medical Bldg 320, University of Nevada, Reno, NV 89557-0046, United States
SO Blood, (1997) 90/12 (4749-4758).
Refs: 53
ISSN: 0006-4971 CODEN: BLOOAW
CY United States
DT Journal; Article
FS 025 Hematology
029 Clinical Biochemistry
LA English
SL English
AB Interferon-γ (IFN-γ) is a potent **inhibitor** of **hematopoiesis** in vitro and has been implicated in the pathophysiology of human bone marrow failure syndromes. IFN-γ both **inhibits cell** cycling and induces expression of the Fas-receptor, resulting in subsequent apoptosis of **hematopoietic** progenitor **cells**. IFN regulatory factor-1 (IRF-1) mediates some of these suppressive affects by activation of downstream inducible genes, such as double-stranded RNA-activatable **protein** kinase and inducible nitric oxide synthase. However, under certain experimental conditions, IFN-γ appears to stimulate **proliferation** of **hematopoietic cells**. Based on the hypothesis that IFN-γ- receptor triggering may activate diverse signaling cascades, we designed experiments to determine which intracellular mechanisms (in addition to the IRF-1 transduction pathway) influence the biologic effects of IRF-1-mediated pathway in KG1a **cells** stimulated with IFN-γ. Using antisense technique, we **inhibited** the IRF-γ. In contrast to the suppressive effects of IFN-γ observed in control **cells**, untreated and IFN-γ-**treated** KG-1a **cells** that were transduced with retroviral vectors expressing IRF-1 antisense mRNA showed enhanced **proliferation**. The increased growth rate was associated with decreased levels of IRF-1 mRNA and **protein** but unchanged levels of IRF-2. We inferred that IFN-γ could also activate a stimulatory transduction pathway that, under specific conditions, may control the cellular response to this cytokine. The family of Stat **proteins** is involved in signal transduction of **hematopoietic** growth factors. We showed that, in KG-1a **cells**, IFN-γ also induced phosphorylation of Stat1 and Stat3, whereas p42 MAP kinase was phosphorylated regardless of the presence of IFN-γ. Using electrophoresis mobility shift assays, IFN-γ enhanced Stat1-Stat1 homodimer and Stat1-Stat3 heterodimer formation, suggesting that, in addition to **inhibitory** signals mediated by IRF-1, IFN-γ may activate **proliferative** signals by phosphorylation of Stat1 and Stat3 **proteins**. The observations made in experiments with KG-1a **cells** were confirmed in primary **hematopoietic cells**. After **inhibition** of the IRF-1 pathway by transduction of an antisense IRF-1 retrovirus into human CD34+ **cells**, IFN-γ produced an aberrant stimulatory effect on **hematopoietic** colony formation. Conversely, in control vector-transduced CD34+ **cells**, the typical **inhibitory** response to IFN-γ may exhibit diverse biologic effects depending on the intracellular balance of transcriptional regulators, in turn

influenced by the activation and differentiation status of the target **cells**.

mucosal surfaces.

L12 ANSWER 25 OF 45 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 97259508 EMBASE
DN 1997259508
TI Relation of platelet abnormalities to thrombosis and hemorrhage in chronic myeloproliferative disorders.
AU Wehmeier A.; Sudhoff T.; Meierkord F.
CS Dr. A. Wehmeier, Medizinische Klinik und Poliklinik, Onkologie/klinische Immunologie, Heinrich-Heine-Univ. Dusseldorf, Moorenstr. 5, 40225 Dusseldorf, Germany
SO Seminars in Thrombosis and Hemostasis, (1997) 23/4 (391-402).
Refs: 156
ISSN: 0094-6176 CODEN: STHMBV
CY United States
DT Journal; General Review
FS 018 Cardiovascular Diseases and Cardiovascular Surgery
025 Hematology
LA English
SL English
AB The chronic myeloproliferative disorders (MPD), predominantly **polycythemia** vera and essential thrombocythemia, are characterized by a high incidence of thromboembolic and, to a lesser degree, hemorrhagic complications. The disease process in chronic MPD affects a pluripotent progenitor **cell** and results in trilineage **hematopoietic proliferation**. Clonal involvement of megakaryocytopoiesis is regarded as the main origin of thromboembolism in MPD and results in abnormal platelet production. These platelets show increased size heterogeneity and ultrastructural abnormalities, and their function in vitro is in many ways impaired with a high degree of individual variability. Elevated levels of platelet-specific **proteins**, increased thromboxane generation, and expression of activation- dependent epitopes on the platelet surface are common in chronic MPD, and may reflect an inappropriate state of platelet activation. Although a variety of platelet receptor deficiencies and some defects of intracellular signaling pathways have been identified, the different platelet defects in MPD could not be traced back to an underlying general pathogenetic mechanism. On progression of chronic MPD to more advanced stages of the disease, the number of platelet abnormalities tend to increase. Cytoreductive drugs may partly improve platelet dysfunction, and platelet **inhibitory** agents **reduce** symptoms of platelet activation. However, neither of these therapeutic principles is able to normalize platelet function in MPD. As an alternative to conventional **treatment**, specific suppression of clonal megakaryocyte growth and recovery of polyclonal **hematopoiesis** may be achieved by biologic agents such as interferon α. Such **treatment** strategies may **prevent** thromboembolic complications together with **hematologic** symptoms and progression of the disease and should be further evaluated in prospective studies.